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10/091,855	03/06/2002	Patrick T. Prendergast	802_003	8597

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BURR & BROWN
PO BOX 7068
SYRACUSE, NY 13261-7068

EXAMINER	
KANTAMNENI, SHOBHA	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 03/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/091,855	PRENDERGAST, PATRICK T.	
	Examiner	Art Unit	
	Shobha Kantamneni	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *NONE* is/are allowed.

6)☒ Claim(s) *18-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment received on 10/11/2005, amended claim 36.

Currently claims 18-44 are pending.

Note: Applicant's elect the species Circiliol which is 5,3',4'-trihydroxy-6,7 dimethoxy flavone as the compound, and gemcitabine as chemotherapeutic agent , and also the election of pancreatic cancer, lung cancer as the type of neoplasia in the reply filed on November 19, 2004.

Applicant's amendment to claim 36 overcomes the objection made in the previous office action for minor informalities.

Applicant's arguments are persuasive, and the rejection of claim 26 under 35 U.S.C 112, second paragraph as being vague is herein withdrawn.

Applicant's arguments have been considered, but not found persuasive, and the rejection of Claims 18-44 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is MAINTAINED. See under response to arguments.

The rejection of claims 18-44 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of lung cancer and pancreatic cancer, **does not reasonably provide enablement for the treatment of neoplasia in general is MAINTAINED**.

Applicant's arguments have been considered and found persuasive, and the rejection of claims 18-21, 23-44 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for chemotherapeutic agent such as antimetabolite

gemcitabine, **does not reasonably provide enablement for the chemotherapeutic agents in general is herein withdrawn**.

Applicant's arguments have been considered and not found persuasive, and the rejection of Claims 18-27, 30-33, 37-44 under 35 U.S.C. 103(a) as being unpatentable over Francis et al. (WO 00/03706) in view of Chinery et al. (WO / 9901118), and further in view of Tsukada et al. (Biochemical and Biophysical Research Communications, Vol. 140, No.3, 1986, pages 832-836) is MAINTAINED. See under response to arguments.

The rejection of claims 28, 34-36 under 35 U.S.C. 103(a) as discussed in the previous office action is MAINTAINED.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 18-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, rejection of record.

(i) In claims 18-44 the recitation "derivatives of said compounds", "metabolites of said compounds", "analogues of said compounds", and "mimic molecules" is vague and indefinite, as it is unclear what other compounds these terms encompass.

(ii) Further, in claim 19 the recitation "precursor molecules of circiliol", "derivatives of circiliol", "metabolites of circiliol", "analogues of circiliol", and "mimic

molecules" is vague and indefinite, as it is unclear what other compounds these terms encompass.

(iii) The phrase "substantially simultaneously" in claim 26 is vague. The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the term, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Response to Arguments:

Applicants argument that "claims must be construed from the standpoint of a person skilled in the relevant art determining whether they particularly point out the subject matter which is covered by the claim" is not persuasive because the recitations, "derivatives of said compounds", "metabolites of said compounds", "analogues of said compounds", and "mimic molecules"; "precursor molecules of circiliol", "derivatives of circiliol", "metabolites of circiliol", "analogues of circiliol", and "mimic molecules" are not clearly defined in the specification, and hence render claims herein indefinite. One of ordinary skill in the art would not ascertain and interpret the metes and bounds of the patent protection desired as to the recitations herein, since one of ordinary skill in the art would clearly recognize that many widely varying groups, and many widely varying compounds could substitute the compounds herein because they would read on the "precursor molecules of circiliol", "derivatives of circiliol", "metabolites of circiliol", "analogues of circiliol", and "mimic molecules" of the ciciliol.

Given the fact that any significant structural variation to a compound would be reasonably expected to alter its properties, e.g., physical, chemical, physiological effects

and functions. Thus, it is unclear and indefinite as to the "derivatives of said compounds", "metabolites of said compounds", "analogues of said compounds", and "mimic molecules"; "precursor molecules of circiliol", "derivatives of circiliol", "metabolites of circiliol", "analogues of circiliol", and "mimic molecules" of circiliol herein encompassed thereby.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of lung cancer and pancreatic cancer, **does not reasonably provide enablement for the treatment of neoplasia in general,** rejection of record. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The specification does not provide sufficient information that all cancers are treatable by using various chemotherapeutic agents and with compounds described in the method claims 18, and 19.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without **undue experimentation**. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required

undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1). The Nature of the Invention:

All of the rejected claims are drawn to an invention which pertains to a method of treating a patient suffering from neoplasia by admininstering compounds such as circiliol and a chemotherapeutic agent. The nature of the invention is complex in that it encompasses the treatment of **all types of cancers** comprising administering circiliol with a wide array of variously chemotherapeutic agents.

(2). Breadth of the Claims:

The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. The claims encompass treatment of **any number of cancers** (**neoplasia**) by administering circiliol with a wide array of variously chemotherapeutic agents. What's more, the scope of the compounds claimed to be useful for the treatment of neoplasia is extremely broad. There are countless possibile chemotherapeutic agents for the treatment claimed.

(3). Guidance of the Specification:

The guidance given by the specification as to how one would administer the claimed compounds to a subject in order to inhibit any type of cancer cell is limited. All

of the guidance provided by the specification is directed toward the treatment of specific cancers such as locally advanced or metastatic pancreatic cancer, larger cell lung cancer line LXFL 529L, and the lung adenocarcinoma cell line LXFA 526L by adminstering Gemicitabine and circiliol.

(4). Working Examples:

Applicant provides *in vitro* examples of the antitumor activity of gemcitabine and circiliol, alone and in combination in the large cell lung cancer line LXFL 529L and the lung adenocarcinoma cell line LXFA 526L in monolayer proliferation inhibition study.

(5). State of the Art:

While the state of the art is relatively high with regard to treating specific cancers, the state of the art with regard to treating **neoplasia** generally is underdeveloped. In particular, there is no known anticancer agent which is effective against all cancers. Carter, et al. (Chemotherapy of Cancer, 2nd ed., 1981) clearly teaches that for the forty known anticancer agents, none are effective against all cancers (pages 362-365). There are compounds that treat a range of cancers, but no one has ever been able to figure out how to get a compound to be effective against cancer generally, or even a majority of cancers. Thus, the existence of such a "silver bullet" is contrary to our present understanding in oncology. This is true in part because cancers arise from a wide variety of sources, such as viruses (e.g. EBV, HHV-8, and HTLV-I), exposure to chemicals such as tobacco tars, genetic disorders, ionizing radiation, and a wide variety of failures of the body's cell growth regulatory mechanisms. Different types of cancers affect different organs and have different methods of growth and harm to the body, and

different vulnerabilities. Even those that affect a single organ are often not generally treatable. For example, the main types of lung cancer are small cell (oat cell), giant cell, clear cell, adenocarcinoma of the lung, squamous cell cancer of the lung, and mesothelioma. There is no such thing as a treatment of these generally because of their diversity. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers generally, evidence that the level of skill in this art is low relative to the difficulty of such a task.

(6). Predictabilitv of the Art:

The invention is directed to treatment of neoplasia in general. It is well established that "the scope of enablement various inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839 (1970). Cancers are especially unpredictable due to their complex nature. Please refer to the discussion of Carter, et al. and the state of the art in (5) that shows the different treatments of cancers. The treatment of one type of cancer could not be necessarily the same for the other type.

(7). The Quantity of Experimentation Necessary:

In order to practice the claimed invention, one of skill in the art would have to first envision a combination of an appropriate pharmaceutical carrier, a dosage for each chemotherapeutic agent and ciciliol, the duration of treatment, route of treatment, etc. and, in the case of human treatment, an appropriate animal model system for one of the claimed compounds. One would then need to test the combination in the model system

to determine whether or not the combination is effective for inhibiting cancer cells. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regarding treatment of cancer with any compound, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above and test the system again. In order to practice Applicant's invention, it would be necessary for one to conduct the preceding experimentation for each type of cancer because, as described by Carter, et al., there is no known drug effective for inhibiting all types of cancer. Therefore, it would require **undue, unpredictable experimentation** to practice the claimed invention to inhibit cancer cells in a mammal by administration of one of the chemotherapeutic agents with circiliol within the claims.

Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, a method for treating a patient suffering from **neoplasia in general** by administering the various chemotherapeutic agents with compounds such as circiliol of the claims is not considered to be enabled by the instant specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The instant invention is drawn to a method of treating a patient suffering from cancers such as pancreatic cancer and lung cancer, comprising administering a chemotherapeutic agent and a compound circiliol.

Claims 18-27, 30-33, 37-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Francis et al. (WO 00/03706) in view of Chinery et al. (WO / 9901118), and further in view of Tsukada et al. (Biochemical and Biophysical Research Communications, Vol. 140, No.3, 1986, pages 832-836), rejection of record.

Francis et al. (WO 00/03706) teach a therapeutic composition comprising a therapeutically efficient amount of a flavonoid type compound of formula (I) in the treatment of tumors with cytotoxic agents. In formula (I), when R_1, R_5 are H, R_4 is OH, and R_6 is phenyl group substituted with 2 OH groups results in circiliol of the instant invention. See page 2, lines 23-30. The chemotherapeutic agents such as gemcitabine, nucleotide analogues such as 5-fluoro Uracil are disclosed. See page 6, line12. It is also taught that the flavonoids can be combined with the major cytotoxic agents used in polychemotherapies for solid tumors. Examples of methods of use of the compounds flavonoids with chemotherapeutic agent gemcitabine for the treatment of bronchial cancer, is also taught. In the chemotherapeutic treatment of cancers with cytotoxic agents, flavonoids can be administered at the start of chemotherapeutic treatments,

either in a single dosage intake or over several days at the start of these treatments depending on the chemotherapeutic protocol. The flavonoid compounds of formula (I) are administered at doses 5 to 50 mg/kg/day. The flavonoid compound and cytotoxic agent can be administered orally, intravenously etc. See page 4, lines 1-10, lines 20-25; lines 30-33, page 6; pages 16, I7. Francis et al. further teach that the flavonoids can be combined with gemcitabine in a treatment regimen for the treatment of pancreatic cancer. See page 39, lines 10-15; page 81, claims 2, 5, and 10. The treatment of Neoplasia in the form of solid tumors such as non-small-cell lung cancers is also taught. See page 14, lines 15-18.

Francis et al. does not explicitly teach the use of flavone such as Circiliol with chemotherapeutic agent for the treatment of Pancreatic cancer, and lung cancer.

Francis et al. do not teach a method of treating pancreatic cancer wherein the compound and/or chemotherapeutic agent are contained in a liposome, and said liposome vehicle can be targeted to tumors.

Chinery et al. (WO/9901118) disclose a method to enhance the cytotoxic activity of an antineoplastic drug comprising administering an effective amount of a antineoplastic drug to a host in combination with an effective amount of an antioxidant. See page 6, lines 4 to 15. The antioxidants increase the effectiveness and decrease the toxicity of antineoplastic agents. The antineoplastic agents include Fluorouracil, Gencitabine, Tamoxifine etc. See page 45, lines 15-20. The antioxidants disclosed include flavonoids, phenolic compounds, and inhibitors of lioxygenases. See page 43, lines 7-10. Chinery et al. further teaches that conditions such as bone cancer, breast

cancer, gastric cancer, pancreatic cancer can be treated using said combination. See page 47, line 5-page 48, line2.

Chinery et al. also teaches that pharmaceutical compositions wherein the active compounds can be in a controlled release formulation, including implants and microencapsulated delivery systems. Biodegradable, biocompatible polymers such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polylactic acid can be used. See page 51, lines 18-21. Liposomal suspensions containing the actives, including liposomes targeted to infected cells with monoclonal antibodies to viral antigens are also disclosed.

Tsukada et al. (Biochemical and Biophysical Research Communications, Vol. 140, No.3, 1986, pages 832-836) teach that flavonoid compounds like Cirsiliol is a potent specific inhibitor for arachidonate 5-lipoxygense and suppressed the growth of leukemia cells in human See abstract; page 834, Fig. 1.

It would have been obvious to a person of ordinary skill in the art at the time of invention to use Circiliol as flavone and combine with gemcitabine as taught by Francis for the treatment of pancreatic cancer. One would be motivated to combine Circiliol a potent inhibitor of arachidonate 5-lipoxygenase as taught by Tsukada with Gemcitabine because (i) Chinery teaches that antineoplastic drugs can be combined with lipoxygenase inhibitor in the treatment of pancreatic cancer (ii) Circiliol is a lioxygenase inhibitor. One would be motivated to use a combination of Circiliol and Gemcitabine for the treatment of pancreatic cancer with the expectation of increasing the effectiveness and decreasing the toxicity of chemotherapeutic agent.

It would have been obvious to a person of ordinary skill in the art at the time of invention to use Cirsiliol as flavone and combine with gemcitabine as taught by Francis for the treatment of lung cancer. One would be motivated to combine Cirsiliol a potent inhibitor of arachidonate 5-lipoxygenase as taught by Tsukada with Gemcitabine because (i) Chinery teaches that antineoplastic drugs can be combined with lipoxygenase inhibitor in the treatment of cancer (ii) Cirsiliol is a lioxygenase inhibitor. One would be motivated to use a combination of Cirsiliol and Gemcitabine with the expectation of treating lung cancer, with increased effectiveness and decreased toxicity of chemotherapeutic agent.

It would have been obvious to a person of ordinary skill in the art at the time of invention to use liposomal suspensions containing Circiliol or chemotherapeutic agent because Chinery teaches liposomal suspension can be used as pharmaceutical carriers for Gemcitabine and flavonoids. The motivation to use liposomal vehicle containing the chemotherapeutic agent or circiliol is with the expectation of delivering the actives more effectively to the infected cells.

Claim 28 is rejected under 35 U.S.C. 103(a), as being unpatentable over Francis et al. in view of Chinery et al. (WO / 9901118), and in view of Tsukada et al. (Biochemical and Biophysical Research Communications, Vol. 140, No.3, 1986, pages 832-836), as applied to Claims 18-27, 30-33, 37-44 above, and further in view of Wang et al. (US 6,608,026), rejection of record.

Francis et al., Chinery, and Tsukada are applied as discussed above.

The references do not teach the administration of radiation treatment.

Wang et al. teach a combination therapy in the treatment of pancreatic cancer by administering a therapeutically effective amount of peptoid,and the antineoplastic agent such as gemcitabine. See column 12, lines 62-66. Wang further teaches that the peptoid, chemotherapeutic agent and/or radiation may be administered concurrently, sequentially, in any order, depending on the nature of the disease, the condition of the patient, and the actual choice of chemotherapeutic agent and/or radiation. See column 11, line 61-column 12, line 8.

It would have been obvious to a person of ordinary skill in the art at the time of invention to administer radiation treatment to a patient undergoing chemotherapy because Wang teaches that chemotherapeutic agent and radiation may be administered concurrently, sequentially in any order. One would be motivated to administer radiation treatment with the expectation of obtaining a beneficial effect of treating cancer more effectively.

Claims 29, and 34-36 are rejected under 35 U.S.C. 103(a), as being unpatentable over Francis et al. in view of Chinery et al. (WO / 9901118), and in view of Tsukada et al. (Biochemical and Biophysical Research Communications, Vol. 140, No.3, 1986, pages 832-836), as applied to Claims 18-27, 30-33, 37-44 above, and further in view of Borisy (US 6,569,853), rejection of record.

Francis et al., Chinery, and Tsukada are applied as discussed above.

The references do not specifically teach that the compounds and/or chemotherapeutic agents are contained in a pharmaceutical formulation which has an enteric coating made of polymers such as poly(lactic-glycolic acid) polyester, cellulose acetate phthalate etc. The references do not teach performing surgery on the patient.

Borisy et al. teach a method of treating a patient having cancer comprising administering chloropromazine and pentamidine. See column 23 , lines 30-35. The treatment can be performed alone or in conjunction with another therapy such as surgery, radiation, chemotherapy. See column 13, lines 55-65. Borisy further teaches that the formulations for oral use include tablets, which may be coated to release the active drug in a predetermined pattern or it may be adapted not to release the active drug substance until after passage of the stomach (enteric coating). The polymers such as methacrylic acid copolymer, cellulose acetate phthalate, hydroxypropyl methylcelluolose phthalate etc. are disclosed for enteric coating. See column 15, lines 33-50.

It would have been obvious to a person of ordinary skill in the art at the time of invention to perform surgery on a patient undergoing chemotherapy because Borisy teaches that chemotherapeutic agent and surgery may be administered in conjunction. One would be motivated to perform surgery with the expectation of obtaining a beneficial effect of treating cancer more effectively.

It would have been obvious to a person of ordinary skill in the art at the time of invention to contain the chemotherapeutic agent in pharmaceutical formulation which has an enteric coating using polymers such as cellulose acetate because Borisy

teaches that the active agents for the treatment of cancer can be contained in a formulation which has enteric coating. One would be motivated to use enteric coating for containing the active agent with the expectation of delaying the disintegration and absorption of the active agent in the gastrointestinal tract and thereby providing a sustained release of the active.

Response to Arguments

Applicant's arguments that "The Office Action contains an assertion that in formula I of WO '706, when R1 and R5 are H, R4 is OH, and R6 is a phenyl group substituted with two OH groups, the resulting compound is circiliol. It is respectfully noted that in addition, it would be necessary that R2 and R3 be methoxy groups. WO '706 discloses for each of the substituents R1 – R6, a number of possible choices, whereby the number of possible combinations of substituents R1 and R6 is extremely large, and yet WO '706 contains no suggestion which would lead a person of skill in the art to make the specific selections which would be necessary in order to arrive at circiliol from within the large number of compounds encompassed by the disclosure in WO '706." This argument is not persuasive because 1) WO'706 teaches that R2 and R3 can be C1-C4 alkoxy group which reads on methoxy groups, and thus the compounds taught by '706 encompass circiliol. Furthermore, it is respectfully pointed out that WO'706 teaches pharmaceutical compositions comprising compounds represented by formula (I) which encompass Circiliol, and also teaches that compounds of formula (I) can be used in the treatment of pancreatic cancer. Thus even though WO '706 et al. does not exemplify Circiliol as preferred compound, it has been well-established that

consideration of a reference is not limited to the preferred embodiments or working examples, but extends to the entire disclosure for what it fairly teaches, when viewed in light of the admitted knowledge in the art, to person of ordinary skill in the art. *In re Boe*, 355 F.2d 961, 148 USPQ 507, 510 (CCPA 1966); *In re Lamberti*, 545 F.2d 747, 750, 192 USPQ 279, 280 (CCPA 1976); *In re Fracalossi*, 681 F.2d 792, 794, 215 USPQ, 570 (CCPA 1982); In re Kaslow, 707 F.2d 1366, 1374, 217 USPQ 1089, 1095 (Fed. Cir. 1983).

Applicant's argument that "A large group of antioxidants are disclosed in pages 25-43 of WO '118, among which are inhibitors of lipoxygenases, but WO '118 does not contain disclosure which would guide a person of skill in the art to make specific selections so as to arrive at circiliol from within the very large number of antioxidants encompassed by the disclosure in WO '118." This argument is not persuasive because applicant is arguing against an individual reference when the rejection was based upon a combination of references.

Applicant's argument that "In the present situation, the present specification demonstrates that the claimed invention achieves results which provide favorable properties which would not have been expected in view of the applied references, and which provides such favorable properties to an extent which would not have been expected in view of the applied references" is not persuasive because 1) Chinery teaches that antioxidants such as lipoxygenase inhibitors increase the effectives and decrease the toxicity of antineoplastic agents, and 2) Circiliol is a lipoxygenase inhibitor.

Thus, one of ordinary skill in the art at the time of invention would have been motivated to use a combination of Circiliol, a potent inhibitor of arachidonate 5-lipoxygenase as taught by Tsukada and Gemcitabine for the treatment of pancreatic cancer with the expectation of achieving favorable properties such as increasing the effectiveness and decreasing the toxicity of chemotherapeutic agent.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period, will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shobha Kantamneni whose telephone number is 571-272-2930. The examiner can normally be reached on Monday-Friday, 7.30am-4.00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shobha Kantamneni, Ph.D
Patent Examiner
Art Unit 1617